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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/883,069	06/14/2001	Shubh D. Sharma	70025-US29743	1720

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/883,069	SHARMA ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-36 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-36 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 24-36 and 38-40 are pending and under examination.

Withdrawn Rejection:

In response to applicants' request for clarification, the 35 USC 101 as stated in the Office action of 6/3/04 no longer applies. Also, the new matter rejection under 35 USC, 112 first paragraph for the variations in at least one of the R1-R7 and non-orthogonal protection of sulfur group in the R groups is withdrawn.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-36 and 38-40, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention for reasons advanced in the last office action.

Response to Arguments

Applicants urge that at page 22, lines 26-27, it is stated that the functional R groups "may be side chains of amino acids". Glycine is an amino acid; its side chain is hydrogen. That hydrogen is intended to be included may be seen at numerous instances with the specification: see, e.g., page 13, lines 27-30, discussing sequences such as Gly-Gly-cys; page 18, line 21, defining "Bbb" as including Gly; and, page 32, Example 11, lines 10 and Example 12, line 29.

In response, the claimed definition for each of R1-R7 is hydrogen ***or alternatively, functional group.*** Thus, hydrogen is not part of the functional group as claimed. Rather, an independent definitions for each of the R1-R7. As stated by applicants above, page 22, lines 26-27 recite amino acids. A functional group may or may not be an amino acid. It may be an organic group as stated at page 22, lines 26-27 for R1. (Only R2, R3 and R4 are recited as amino acids.) As applied to e.g., formula I of claim 21, it is not clear as to the attachment of (R4), if glycine, to the structure of (I).

B) Applicants assert that at the bottom of page 6 of the Detailed Action, it is stated that cys can react with each other

in a given library or cross-link with other cys in other libraries. As a general statement, this is true. But urge that central to the invention is that both orthogonal and non-orthogonal protecting groups for the reactive sulfur in cys are provided to avoid just this eventuality. See, e.g., page 8, Lines 17-22, discussing as an object of the invention "to provide methods for synthesis of peptides wherein the peptides contain one or more reactive SH groups forming a part of a metal ion-binding domain, whereby the reactive SH groups are protected during synthesis, and are deprotected only upon complexing the peptides with a metal ion.

In response, while the protection and deprotection of cys might be applied during synthesis, however, it is not apparent from the claimed library per se, as to the final composition of the library. There is nothing in the claimed library to differentiate a protected and deprotected cys residues in each of the R groups. The claims simply recite "functional group". Furthermore, the claimed functional group is not limited to only cys containing group, rather to a claim of undefined structure. Applicants argue that there is no requirement in patent law that any given library must have the ability to screen for any (or every) desired target. It is further argued that the examples provide clear guidance and direction on how the claimed

invention may be employed. See, e.g., Example 5, page 26, discussing a library based on the tetrapeptide His-phe-Arg-Trp; (Example 6 and Example 7); Example 10, pages 30-32, discussing library based on general structure Ac-His-xaa-cys-Trp-NH2, Example 11, page 32, discussing human neutrophil elastase libraries of the general structure R-Aaa-Bbb-Cys-Val-N2 and the other argued Examples of known target to which at least one of the R groups binds to the known target.

In reply, there is no requirement that a library be screened for each and every compound. Rather, the law requires that applicants provide a reasonable assurance that the claimed library is capable of accomplishing its result. The court (University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993) found a lack of written description because, although the patentee provided a process a for obtaining human insulin encoding CDNA, the patent did not disclose a human insulin encoding CDNA made by the process, and the patent did not actually teach the structure or physical characteristics of the human insulin encoding CDNA. It seems to parallel the instant invention. The specific examples appear not to identify a metallo-peptide(s)from the library.

It is not controverted that the Examples describe the library in specific structures reacting with specific receptors (target). The issue is whether the specific examples, at the time of filing, correlate to possession of the huge scope of the claimed library. The specification provides a huge definition for each of the R variables. Each variables can be represented either, singly or combinations in each of the claimed library. It is not readily apparent in the Examples whether the single tetrapeptide structure, is applicable for the huge scope, as claimed. Applicants may not preempt an unduly large filed by the expedient of making broad prophetic statements in the specifications and claims unless the accuracy of such statements is sufficiently supported by well-established chemical principles or by sufficient number of examples.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24-36 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sharma (U.S. 6,027,711) ('711 patent).

Applicants state that pursuant to MPEP 706.02(1)(3), the undersigned attorney of record for Applicant states:

The instant application number 00/883,069 and co-pending application 09/483,837 were, at the time the invention of instant application number 09/883,069 was made, owned by Palatin Technologies. Inc. The parent of co-pending application 09/483,837 (issued as U.S. Patent No. 6,027,711, with 09/483,837 being a divisional thereof is shown as owned by RhoMed Incorporated, since June 25, 1996, RhoMed Incorporated has been a wholly-owned (100%) subsidiary of Palatin Technologies, Inc.)

In view of applicants' representative Statement Concerning Common Ownership at page 10 of the instant REMARKS, the rejection no longer applies.

Claims 24-36 and 38-40, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Hnatowich et al (U.S. 5,980,861) for reasons set forth in the last Office action.

Response to Arguments

Applicants argue that Hnatowich does not disclose libraries synthesized by use of orthogonal sulfur atom-protecting

groups as defined in the specification. The term is argued as defined at page 14, line 20 bridging page 16, line 18, and specifically at page 14, starting at line 20.

> The SH protecting group is chosen such that (a) the synthesis of peptide derivatives with S-protecting group is compatible with methods of solution and solid phase peptide synthesis, so that the S-protecting group is stable during synthetic procedures, and (b) the S-protecting group can be deprotected in situ, without cleavage from the resin in the case of solid phase synthesis, during the metal complexation step.

It is additionally argued that claim 24, as amended, contains a specific limitation, "wherein each constituent metallopeptide library member is made by a synthetic process wherein the sulfur atom (S) is protected by an orthogonal sulfur atom-protecting group compatible with peptide solid phase synthesis and removable without cleaving the peptide from solid phase." To the extent that the prior Office Action suggests that Fmoc may be an orthogonal sulfur-protecting group, Applicant asserts that Fmoc is an amino protecting group, not a sulfur protecting group. While it is certainly well known that Fmoc may be employed in peptide synthesis, Fmoc was discussed in the prior Amendment to demonstrate that the S-acetyl thioester group employed by Hnatowich is not compatible with peptide synthesis, because piperidine, which is commonly used to

cleave Fmoc groups from amino functions during peptide synthesis, would also hydrolyze a thioester bond. Thus the S-acetyl/ thioester group employed by Hnatowich is not an orthogonal sulfur protecting group as defined by Applicants.

In reply, it is immaterial whether the process uses an orthogonal or non-orthogonal protecting groups, especially when the definition relates to function rather, than structure. The fact that Hnatowich discloses a similar library suffices the finding of obviousness. It would be within the ordinary skill in the art to determine whether a protecting group is compatible during peptide synthesis. The fact is peptide synthesis has markedly advanced that an automated synthesizer is now used.

When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different process. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the

recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and the obtain prior art products and make physical comparisons therewith." In re Brown, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Double Patenting

Claims 24-36 and 38-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41, 43-51, 53-59 and 63-81 of copending Application No. 09/483,837 ('837 application) for reasons of record.

Response to Arguments

It is argued that with the amendment to claim 24, which includes the limitation "the sulfur atom (S) is protected by an orthogonal sulfur atom-protecting group compatible with peptide solid phase synthesis and removable without cleaving the peptide from solid phase. There are no claims in co-pending application 09/483,837 drawn to orthogonal protecting groups. To the extent that the Office relies upon the disclosure of specific protecting groups such as S-aminopropyl cysteine or S-aminoethyl cysteine as covered by the broad claimed orthogonal protecting groups, Applicants respectfully traverses this ground. There is no disclosure or suggestion in co-pending application 09/483,837 that these specific protecting groups can be removed to result in a reactive -SH group. The only disclosure of either S-aminopropyl cysteine or S- aminoethyl cysteine is as a "basic residue" which may be employed (see column 38, lines 63-67 and

column 39, lines 10-14 in the '711 patent), and which may in some instances contribute a nitrogen (N) to binding (see column 37, lines 57-61 and column 38, lines 63-67 in the '711 patent). There is no teaching or suggestion that either residue may be deprotected such that it contributes a sulfur (S) for binding.

In reply, col. 38, line 60 clearly states an S-aminoethyl-cys or other synthetic amino acids. The specific recitation of S-aminoethyl cys is sufficient to support the finding of obviousness.

See further the discussion under Hnatowich above, as to the product by process arguments.

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571)272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
March 4, 2005